Hill coefficients CAF 2.14 ± 0.16, HF 2.53 ± 0.14, P<0.05). Consistently, the results of real time PCR and western blot demonstrated that captopril significantly downregulated the expression of apamin sensitive SK channels (SK3 mRNA: CAF 2.10 ± 0.9, n = 6 vs HF 8.40 ± 2.10, n = 6; SK3 protein: CAF 0.40 ± 0.07, n = 6 vs HF 0.56 ± 0.09, n = 6).

CONCLUSIONS Captopril significantly downregulated the sensitivity of SK channels to $[Ca^{2+}]i$ and the SK3 channels expression in HF, and reversed the SK channels remodeling.

GW26-e1586

AMPK attenuates proliferation of cardiac fibroblast via regulating TGF-β1/Smad pathways

Yili Chen,[1] Chunxi Lin,[1] Yufang Zhong,[2] Guiying Lu,[1] Yuedong Ma,[1] Huiling Huang[1]
[1]Department of Cardiology, the First Affiliated hospital of Sun Yat-Sen University; [2]Department of Nephrology, the First Affiliated hospital of Sun Yat-Sen University

OBJECTIVES AMP-activated protein kinase (AMPK) exerts inhibitory effects on cardiac hypertrophy. However, the mechanism remains unclear. The aim of the present study was to investigate the effects of AMPK on angiotensin II (AngII) -induced proliferation of cardiac fibroblast and the mechanisms involved.

METHODS Proliferation of cardiac fibroblast was induced by angiotensin II (AngII). Cardiac fibroblasts were treated with the specific AMPK activator 5-aminoimidazole-4-carboxamide ribonucleoside (AICAR, 0.5 mmol/L) and the specific AMPK antagonist Compound C (1 umol/L), and then stimulated with AngII (1 umol/L). Cell proliferation and the DNA synthesis were measured by MTT assay and EdU incorporation assay. TGF-β1 and Smad2, 3, 4 mRNA and protein expression was detected using Real-Time PCR and western blot analysis.

RESULTS Activation of AMPK by AICAR could inhibit AngII-induced proliferation of cardiac fibroblasts, manifesting decreased DNA synthesis and collagen production ($P<0.05$). Moreover, AngII significantly increased the mRNA and protein expression of TGF-β1 and Smad2, 3, 4 ($P<0.05$). AMPK activation markedly reversed the elevated TGF-β1 and Smad2, 3, 4 mRNA and protein levels ($P<0.05$). Furthermore, Treatment of proliferated cardiac fibroblasts with Compound C blunted the effects of AMPK on proliferation of cardiac fibroblasts and changes to the TGF-β1/Smad pathway ($P<0.05$).

CONCLUSIONS AMPK activation could attenuate proliferation of cardiac fibroblast induced by AngII, which may be due to the inhibition of TGF-β1/Smad pathways.

GW26-e4768

Improved Recovery After Myocardial Ischemic Infarction by Copper Supplementation

Pengfei Han,[1] Xiang Zhou,[1] Wenjing Zhang,[1] Qipu Feng,[1] Ying Xiao,[1] Xiaorong Sun,[1] Xinmei Zhao,[1] Haiying Fu,[1] Y. James Kang[1,2]
[1]Regenerative Medicine Research Center, West China Hospital, Sichuan University, Chengdu, Sichuan, China; [2]Department of Pharmacology and Toxicology, University of Louisville School of Medicine, Louisville, Kentucky, USA

OBJECTIVES Depressed angiogenesis due to ischemic injury leads to myocardial infarction. Copper (Cu) is involved in angiogenesis and ischemia causes copper loss in the heart. The present study was undertaken to test the hypothesis that Cu supplementation improves myocardial angiogenesis, leading to regression of myocardial ischemic infarction in Rhesus monkey model.

METHODS Coronary artery ligation was used to produce myocardial ischemia and the monkeys developed myocardial infarction 4 weeks after ischemia. A newly developed ultrasound contrast microbubble composed of Cu-albumin coated structure was used to specifically deliver Cu into the infarct area. The treatment was performed twice a week for 4 weeks.

RESULTS This procedure effectively increased Cu concentrations in the infarct area and activated the angiogenesis factors including vascular endothelial growth factor (VEGF), VEGF receptor-1 (VEGFR-1), and other relevant factors. Along with these changes, myocardial infarct size was significantly decreased and the density of myocardial microvessels was significantly increased. In addition, cardiac function was significantly recovered, as evidenced by increased ejection fraction (EF) values and decreased end-systolic volume (ESV) measured by echocardiography.

CONCLUSIONS This study thus demonstrated that Cu supplementation improved cardiac structural and functional recovery after ischemic infarction.

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Discovery of a new conduction substrate associated with atrioventricular node-anterior extension pathway

Fan Wang, Shuo Zhang
Second Affiliated Hospital of Harbin Medical University

OBJECTIVES The atrioventricular node(AVN) plays a role in conducting action potentials at an appropriate conduction velocity from atria to ventricles. Its complex anatomical structures and functional longitudinal dissociations are considered important in delayed conduction and AVN reentrant tachycardia (AVNRT). Inferior nodal extensions(INE) are part of the AVN. It is thought that these extensions may be involved in slow-pathway conduction and are part of the underlying circuitry that causes AVNRT. Some other conduction tissue shared the same origin layers with AVN distribute around the two valve annulus. The retroaortic node defined as the enlargement of this node-like tissue is located on the right side of the atrium parallel with the aorta. The potential electrophysiological function of these node-like tissues is still unknown. Understanding their detail anatomical structure, histological features and electrophysiological behavior are significant to clear the complex conduction characteristics of the AV junction.

METHODS Adult rats(n=6), mice(n=5) and rabbit(n=5) were used. Serial sections from the entire AV junction were obtained. Masson's trichrome stain was performed on AVN regions to assess for fibrous tissue. Three connexins(Cx) proteins including Cx43, Cx40 and Cx45 which dominate the electronic conduction of the heart and three main ion channels($Na_v1.5$, $Ca_v3.1$ and HCN4) participating the depolarization of myocardial cell were immunohistochemically labeled. Serial sections were used to reconstruct a 3D computational model of the anatomy of the AV junction which display the different histological features at different levels.

RESULTS There appears to be an anterior extension of the AVN which connect retroaortic node and AVN. The anterior node extension (ANE), compact node and INE express the same connexin isoforms. $Na_v1.5$ labeling was abundant in the atrial and ventricular myocardium. $Na_v1.5$ labeling presents at a reduced level in the compact node, ANE and INE. $Ca_v3.1$ and HCN4 expression were mainly expressed in the $Na_v1.5$ reduced area. Further, connections between the atria and inferior extension occur indirectly via small branches. However, this was distinct from the connection pattern that we observed between the atria and ANE, which was direct.

CONCLUSIONS We conclude that the retroaortic node connect with ANE forming ANE which suggests there would be direct electric conduction between them. Characteristics of these structures are conserved among various species including rat, mouse and rabbit as we had proven. ANE, AVN and INE have nearly the same electronic level and action potential level structure basic that highlight they would have the same conduction properties, but there are different connection patterns in atrium between them that suggests there would be the subtle conduction velocity difference after accept the impulse, which provide a new location and substrate of conduction that may present new insights on mechanisms underlying normal AV conduction and AVNRT.

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AVE 0991, Nonpeptide angiotensin-(1-7) analogue, modulates cardiac hypertrophy via reducing oxidative stress

Yili Chen,[1] Yufang Zhong,[2] Chunxi Lin,[1] Guiying Lu,[1] Huiling Huang,[1] Yuedong Ma[1]
[1]Department of Cardiology, the First Affiliated hospital of Sun Yat-Sen University; [2]Department of Nephrology, the First Affiliated hospital of Sun Yat-Sen University

OBJECTIVES AVE 0991, the nonpeptide angiotensin-(1-7) (Ang-(1-7)) analog, is recognized as having beneficial cardiovascular effects. However, the mechanisms have not been fully elucidated. This study was designed to investigate the effects of AVE 0991 on cardiac hypertrophy and the mechanisms involved.

METHODS Mice were subjected to aortic banding (AB) to induce cardiac hypertrophy. *After treatment with* AVE 0991 (20 mg·kg·day (-1)) for four weeks, indices of cardiac hypertrophy and heart function were measured by echocardiography, histological analyses and quantitative